

Serial No.: 10/798,592
Group Art Unit 1615
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IN THE CLAIMS:

1. (Currently Amended) A medical article comprising:
 - a first nitric oxide donor compound; and
 - a second nitric oxide donor compound, said second nitric oxide donor compound differing from said first nitric oxide donor compound,wherein said medical article is adapted, after placement at a delivery position on or within the body of a patient, for local delivery of ~~one or more of~~ said first nitric oxide donor compound and a nitric oxide product of said first nitric oxide donor compound and for local delivery of ~~one or more of~~ said second nitric oxide donor compound and a nitric oxide product of said second nitric oxide donor compound.
2. (Original) The medical article of claim 1, wherein said medical article is selected from vascular medical devices, urological medical devices, biliary medical devices, gastrointestinal medical devices, medical devices adapted for placement at surgical sites and medical devices adapted for placement on skin wounds or openings.
3. (Original) The medical article of claim 1, wherein said first and second nitric oxide donor compounds are selected from organic nitrates, O-nitrosylated compounds, S-nitrosylated compounds, nonoate compounds, inorganic nitroso compounds, sydnonimines, and L-arginine.
4. (Original) The medical article of claim 1, wherein said first and second nitric oxide donor compounds are S-nitrosylated compounds.
5. (Currently Amended) The medical article of claim 1, wherein said first nitric oxide donor compound has a ~~short half-life~~ that is greater than a half-life of and said second nitric oxide donor compound ~~has a long half-life~~.

Serial No.: 10/798,592
Group Art Unit 1615
Examiner Isis A. D. Ghali

6. (Original) The medical article of claim 5, wherein said short half-life compound is selected from diethylamine nonoate, (E)-2-[(E)-hydroxyimino]-6methoxy-4-methyl-5-nitro-3-hexenamide, 3-(aminopropyl)-1-hydroxy-3-isopropyl-2-oxo-1-triazene, 3-ethyl-3-(ethylaminoethyl)-1-hydroxy-2-oxo-1-triazene and nitroso-N- acetylpenicillamine.
7. (Previously Presented) The medical article of claim 5, wherein said long half-life compound is selected from S-nitrosogluthathione, polyethylene glycol-NO-nucleophile hydrogels and polyurethane and poly(vinyl chloride) containing nitric oxide-releasing diazeniumdiolate moieties.
8. (Original) The medical article of claim 1 wherein, upon placement at said delivery position, said first nitric oxide donor compound has a half-life that is at least 10 times as great as a half-life of said second nitric oxide donor compound.
9. (Currently Amended) The medical article of claim 1 wherein, upon placement into the a vasculature within said body of said patient, said first nitric oxide donor compound has a half-life that is at least 10 times as great as a half-life of said second nitric oxide donor compound.
10. (Original) A method of increasing local nitric oxide concentrations in the body comprising placing the medical article of claim 1 at said delivery position on or within the body of said patient.
11. (Original) The medical article of claim 1, wherein at least one of said first and second nitric oxide donor compounds is adsorbed or attached to a region of said medical article.

Serial No.: 10/798,592
Group Art Unit 1615
Examiner Isis A. D. Ghali

12. (Original) The medical article of claim 1, wherein at least one of said first and second nitric oxide donor compounds is disposed within a polymer matrix.
13. (Original) The medical article of claim 1, wherein at least one of said first and second nitric oxide donor compounds is disposed within a solution or fluid dispersion.
14. (Original) The medical article of claim 1, said first nitric oxide donor compound having a first mechanism for nitric oxide release, and said second nitric oxide donor compound having a second mechanism for nitric oxide release differing from said second mechanism.
15. (Original) The medical article of claim 14,
wherein said first nitric oxide donor compound has greater activity than said second nitric oxide donor compound with respect to at least one action selected from vasodilation, platelet aggregation inhibition, vascular inflammation reduction, smooth muscle proliferation reduction, and endothelial cell protection and
wherein said second nitric oxide donor compound has greater activity than said first nitric oxide donor compound with respect to at least one other action selected from vasodilation, platelet aggregation inhibition, vascular inflammation reduction, smooth muscle proliferation reduction, and endothelial cell protection.
16. (Original) The medical article of claim 15, wherein said first nitric oxide donor compound has greater vasodilation activity than said second nitric oxide donor compound and said second nitric oxide donor compound has greater platelet aggregation inhibition activity than said first nitric oxide donor compound.
17. (Original) The medical article of claim 14, wherein said first nitric oxide donor compound releases nitric oxide at a higher rate than said second nitric oxide donor compound when contacted with a first tissue, and said second nitric oxide donor compound releases

Serial No.: 10/798,592
Group Art Unit 1615
Examiner Isis A. D. Ghali

nitric oxide at a higher rate than said first nitric oxide donor compound when contacted with a second tissue.

18. (Original) The medical article of claim 17, wherein said first tissue is blood and said second tissue is vascular tissue.

19. (Original) The medical article of claim 14, wherein said first and second nitric oxide donor compounds are S-nitrosothiol compounds.

20. (Original) The medical article of claim 19, wherein said first nitric oxide donor compound is directly susceptible to metal ion catalyzed release, and wherein said second nitric oxide donor compound is substantially susceptible to metal ion catalyzed release only after having been converted to a third S-nitrosothiol compound.

21. (Original) The medical article of claim 20, wherein said first compound is S-nitroso-DL-penicillamine and said second compound is S-nitrosoglutathione.

22. (Original) The medical article of claim 14, wherein said medical article further comprises a component selected from an amino acid, a metal ion and an enzyme.

23. (Withdrawn) A method of treating an atherosclerotic lesion comprising:
 exposing said lesion to a first concentration of nitric oxide effective to reduce the number of cells within the lesion; and
 subsequently exposing said lesion to a second concentration of nitric oxide effective to inhibit restenosis, said second concentration being lower than said first concentration.

24. (Withdrawn) The method of claim 23, wherein said lesion is exposed to said first concentration of nitric oxide for a first period ranging from 12 hours to 84 hours and said

Serial No.: 10/798,592
Group Art Unit 1615
Examiner Isis A. D. Ghali

lesion is subsequently exposed to said second concentration of nitric oxide for a second period ranging from 3 to 12 weeks.

25. (Withdrawn) The method of claim 24, wherein said first period ranges from 24 to 48 hours.

26. (Withdrawn) The method of claim 24, wherein said second period ranges from 4 to 6 weeks.

27. (Withdrawn) The method of claim 23, wherein said first and second concentrations are provided by a medical device placed at said lesion.

28. (Withdrawn) The method of claim 27, wherein said medical device comprises: (a) a first nitric oxide donor compound; and (b) a second nitric oxide donor compound, said second nitric oxide donor compound differing from said first nitric oxide donor compound.

29. (Withdrawn) The method of claim 28, wherein, upon placement at said lesion, said first nitric oxide donor compound has a half-life that is at least 10 times as great as a half-life of said second nitric oxide donor compound.

30. (Withdrawn) The method of claim 27, wherein said first and second nitric oxide donor compounds are selected from organic nitrates, O-nitrosylated compounds, S-nitrosylated compounds, nonoate compounds, inorganic nitroso compounds, sydnonimines, and L-arginine.

31. (Withdrawn) The method of claim 27, wherein said medical device comprises:

(a) a first nitric oxide donor compound, said first nitric oxide donor compound being adsorbed to, attached to or disposed within a first composition and

Serial No.: 10/798,592
Group Art Unit 1615
Examiner Isis A. D. Ghali

(b) a second nitric oxide donor compound, said second nitric oxide donor compound being adsorbed to, attached to or disposed within a second composition which is chemically distinct from first composition,

wherein the first and second nitric oxide donor compounds can be the same or different.

32. (Withdrawn) The method of claim 31, wherein said first composition is a first polymer matrix within which said first nitric oxide donor compound is disposed, and wherein said second composition is a second polymer matrix differing from said first polymer matrix within which said second nitric oxide donor compound is disposed.

33. (Withdrawn) The method of claim 31, wherein said first and second nitric oxide donor compounds are selected from organic nitrates, O-nitrosylated compounds, S-nitrosylated compounds, nonoate compounds, inorganic nitroso compounds, sydnonimines, and L-arginine.

34. (Withdrawn) The method of claim 27, wherein said medical device is selected from stents, infusion catheters, intraluminal paving devices.

35. (Withdrawn) A method of increasing local nitric oxide concentrations within two or more bodily tissues comprising:

providing a medical article comprising (a) a first nitric oxide donor compound; and (b) a second nitric oxide donor compound, wherein said first nitric oxide donor compound has a first mechanism for nitric oxide release, and wherein said second nitric oxide donor compound has a second mechanism for nitric oxide release differing from said first mechanism; and

placing said medical article at a delivery position on or within the body of patient.

Serial No.: 10/798,592
Group Art Unit 1615
Examiner Isis A. D. Ghali

36. (Withdrawn) The method of claim 35, wherein said first nitric oxide donor compound releases nitric oxide at a higher rate than said second nitric oxide donor compound when contacted with a first tissue, and said second nitric oxide donor compound releases nitric oxide at a higher rate than said first nitric oxide donor compound when contacted with a second tissue.

37. (Withdrawn) The method of claim 35, wherein said first and second nitric oxide donor compounds are S-nitrosothiol compounds.

38. (Withdrawn) The method of claim 37, wherein said first nitric oxide donor compound is directly susceptible to metal ion catalyzed release and said second nitric oxide donor compound is susceptible to substantial metal ion catalyzed release only after being converted to a third S-nitrosothiol compound.

39. (Withdrawn) The method of claim 38, wherein said first compound is S-nitroso-DL-penicillamine and said second compound is S-nitrosoglutathione.